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# Maxillary sinus lift with solely autogenous bone compared to a combination of autogenous bone and growth factors or (solely) bone substitutes. A systematic review

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*Abstract.* Literature regarding the outcome of maxillary sinus floor elevation to create sufficient bone fraction to enable implant placement was systematically reviewed. Bone fraction and implant survival rate were assessed to determine whether grafting material or applied growth factor affected bone fraction. Trials where sinus floor elevations with autogenous bone (controls) were compared with autogenous bone combined with growth factors or bone substitutes, or solely with bone substitutes (test groups) were identified; 12 of 1124 fulfilled all inclusion criteria. Meta-analyses comparing the bone fraction after applying: autogenous bone; autologous bone with growth factors (platelet rich plasma); or autogenous bone and bone substitutes (bovine hydroxyapatite, bioactive glass, corticocancellous pig bone) revealed no significant differences in bone formation after 5 months. A significantly higher bone fraction was found in the autogenous bone group compared to the sole use of β-tricalciumphosphate ($P = 0.036$). The one-year overall implant survival rate showed no significant difference between implants. Bone substitutes combined with autogenous bone provide a reliable alternative for autogenous bone as sole grafting material to reconstruct maxillary sinus bony deficiencies, for supporting dental implants after 5 months. Adding growth factors (platelet rich plasma) to grafting material and the sole use of β-tricalciumphosphate did not promote bone formation.

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Application of dental implants to support prosthetic constructions has evolved into a viable alternative to conventional prosthetic procedures. Implant procedures in the posterior maxilla often pose a problem due to insufficient pre-existing bone fraction[13,15,36]. This is not restricted to edentulous patients, but is also often observed in partially dentate patients needing an implant-based prosthodontic reconstruction in the posterior region of the maxilla. The problem of an insufficient level of bone[4] to allow for reliable primary placement of implants can be solved by a maxillary sinus floor elevation procedure using autogenous bone, bone substitutes or a mixture of autogenous bone and bone substitutes as grafting materials. Augmentation of the maxillary sinus floor with an autogenous bone graft, introduced by Boyne & James[3] and Tatum[30], is a commonly used method for increasing vertical bone height for insertion of dental implants.

During the maxillary sinus floor elevation procedure, the space created between the residual maxillary ridge and the elevated Schneiderian membrane is usually filled with grafting material[7,38]. In this way, a bone fraction is created that may allow for reliable implant placement, either simultaneously with the elevation procedure when the residual ridge allows for primary implant stability or as a second stage after healing of the grafted site [3,13,22].

For sinus floor augmentation, autogenous bone is the most commonly used material and is still considered the gold standard[12,13,16,34], although numerous alternative materials have been used with variable results. Recent studies have demonstrated that the mere lifting of the sinus mucosal lining and simultaneous placement of implants also can result in bone formation without the use of a grafting material[17]. Currently, this technique only is applied for conditions allowing for sufficient primary stability of implants during placement and a sufficient width of the alveolar crest but not for reconstruction in horizontal and vertical directions.

Autogenous bone grafts are the most widely used[6]. Autografts are popular because they have osteogenic, osteoinductive, osteoconductive properties, a high number of viable cells and are rich in growth factors. The viable cells consist of osteoblasts, undifferentiated mesenchymal cells, monocytes and osteoclast precursor cells. These cells participate in the remodelling and formation of the new bone[12]. Alternatives such as bone substitutes do not provide the cellular elements necessary for osteogenesis and are only osteoconductive[32]. These alternatives are synthetic or most organic material has been removed from the substitute material during the fabrication process.

Donor site morbidity is a problem associated with bone-harvesting techniques, which can be reduced or avoided when using bone substitutes[39]. Whether autogenous bone should still be considered as the grafting material of choice can be questioned. Can autogenous bone be (partially) replaced by bone-substitutes? The length of healing time required before placing implants in a site grafted with a bone substitute remains unclear (usually a site reconstructed with a bone substitute requires longer before implant placement than a site reconstructed with autogenous bone). Also, whether a bone substitute can be applied solely or always has to be combined with autogenous bone remains unclear. Clinicians are keen to speed up healing, and the effect of using platelet rich plasma (PRP) has been studied for its presumed effect of speeding up bone regeneration. It has been speculated that growth factors that are present in PRP could enhance healing of the grafts and might counteract resorption after augmentation[1,18].

The effect of maxillary sinus floor elevation on the survival of endosseous dental implants has been reviewed systematically in general terms in the past[2,14,37], but a detailed analysis of the efficacy of using an autogenous bone graft compared with bone substitutes and bone growth factors on bone formation and implants was not carried out. The authors of the reviews discussed solely autogenous bone or only bone substitutes, but did not compare the treatment outcome of various grafting materials with autogenous bone serving as a control. Retrospective studies, case reports, prospective and cohort studies were included in the reviews mentioned above, so the conclusions of the reviews were not based on the most reliable type of clinical studies. The consensus of the sixth European workshop on periodontology[9,33] emphasized the research need to answer comparative questions to establish the clinical benefit of bone augmentation with respect to alternative treatments and to compare different treatments in terms of, amongst others, effectiveness, adverse effects and morbidity. In a recent Cochrane review, Esposito et al.[8] discussed the effectiveness of sinus lift procedures for dental implant rehabilitation. No statistically significant difference was observed for any of the interventions evaluated. Conclusions are based on a few trials, usually underpowered, with short follow-up periods, and often judged to be at high risk of bias, therefore they should be viewed as preliminary and interpreted with caution. Analysis of the efficacy of using an autogenous bone graft compared with bone substitutes and bone growth factors on bone formation and implant survival was not studied.

The aim of this study was systematically to review the literature regarding the treatment outcome of residual maxillary ridges needing maxillary sinus floor elevation surgery to create sufficient bone fraction for reliable implant placement in humans. The objectives of this systematic review were to assess the bone fraction and implant survival rate and to determine whether the bone fraction is affected by the grafting material or growth factor applied.

## Material and methods

For this review, a thorough search of the literature was conducted in the electronic databases MEDLINE (1979–September 2010, via PUBMED) and EMBASE (1987–September 2010). Studies in which patients were treated with a maxillary sinus floor elevation with autogenous bone as a control group were searched. Three types of intervention were considered: solely bone substitutes; autogenous bone in combination with bone substitutes; and autogenous bone in combination with growth factors. Outcome measures were bone fraction after healing period and implant survival.

The search strategy used was a combination of MeSH terms and free text words; 'Maxilllary sinus lift'[Mesh] OR (sinus augmentation) OR (sinus floor elevation) OR (maxillary sinus lift) OR (sinus graft) AND 'Dental Prosthesis, Implant-Supported'[Mesh] OR 'Implants, Experimental'[Mesh] OR 'Prostheses and Implants'[Mesh] OR 'Dental Implants'[Mesh] OR 'Dental Implantation, Endosseous'[Mesh] OR 'Dental Abutments'[Mesh] OR (alveolar atrophy) OR (implant*) OR (dental implant*) OR (oral implant*) AND (Humans[Mesh]). No language restrictions were applied.

The references of each relevant review and eligible study were checked. The titles and abstracts of the searches were assessed independently by two examiners. Full text documents were obtained for possibly relevant articles. Manual searches of the bibliographies of all full text articles and related reviews selected from the electronic search were also performed and completed the review.

Longitudinal studies (randomized controlled trials, cohort studies) were consid-

ered for evaluation. Patients with maxillary atrophy, who had undergone a maxillary sinus lift, were included. Only studies in which autogenous bone was used as a control group were chosen as autogenous bone is considered the gold standard and is considered to be accompanied by the highest level of bone growth, at least during the first months after grafting. Including an autogenous bone group as a control also better allows for comparison of the various studies. There were three types of intervention: solely bone substitutes; autogenous bone in combination with bone substitutes; autogenous bone in combination with growth-factors. Outcome measures were bone fraction after the healing period and implant survival after at least 1-year follow-up in patients with alveolar atrophy treated with a sinus lift procedure. This sinus lift was performed with autogenous bone alone (control group) compared to autogenous bone in combination with growth factors or bone substitutes, or solely with bone substitutes (test groups). Retrospective studies, studies with an inadequate study design, or an unclear intervention, case series, technical reports and reviews were excluded. Articles that were not topic related, with no full texts were excluded. Language was not restricted.

Two reviewers independently assessed the methodological quality using the forms 'quality assessment of a cohort study' and 'quality assessment of a randomized clinical trial' developed by the Dutch Cochrane Centre, a centre of the Cochrane Collaboration (www.cochrane.nl). These two validity tools consist of eight and nine items, respectively, which have to be scored with a plus, minus or a question mark. It was decided that studies scoring four or more plusses were considered methodologically acceptable. The two observers independently generated a score for the included articles. No blinding for author, institute or journal was performed. The main items of quality assessment were: Was the study randomized and the randomization procedure clearly stated? How good was the allocation concealment? Was a clear description of study group, inclusion and exclusion criteria, intervention and outcomes given? Was a clear description of withdrawals and drop outs given? Disagreements on validity assessment were resolved by discussion.

For each study the following data were extracted and recorded on a data sheet: study design (randomized controlled trial or prospective cohort study); treatment (control versus test); number of patients; type of patient (edentulous or not); details of type of intervention; number of sinus floor elevations and implants placed; details of the outcomes (new bone formation) and implant survival; follow-up time.

### Statistical analysis

With respect to the quality assessment, agreement between the two reviewers regarding eligible studies was expressed using Cohen's unweighted kappa. Failure rates were calculated by dividing the number of events (failures or complications) in the numerator by the total exposure time (implant time) in the denominator. The numerator was in all cases extracted directly from the publication or was provided by the authors of the original papers in cases in which only a part of the full sample was taken into consideration. The exposure time was extracted and calculated by multiplying the mean follow-up time by the number of implants available in the given statistical analysis. The mean follow-up was directly extracted from the articles. For each study, event rates for implants were calculated by dividing the total number of events by the implants' exposure time in years.

A meta-analysis was carried out for evaluating bone fraction. Random effect models were created and a standardized weighted mean difference was used to evaluate bone fraction. Meta-analysis was performed using the statistical software package 'Meta-analysis' (Comprehensive Meta-analysis Version 2.2, Biostat, Englewood NJ, USA (2005), www.meta-analysis.com).

## Results

The search in MEDLINE and EMBASE provided 1124 articles reporting maxillary sinus floor elevation in combination with dental implant placement. Fig. 1 outlines

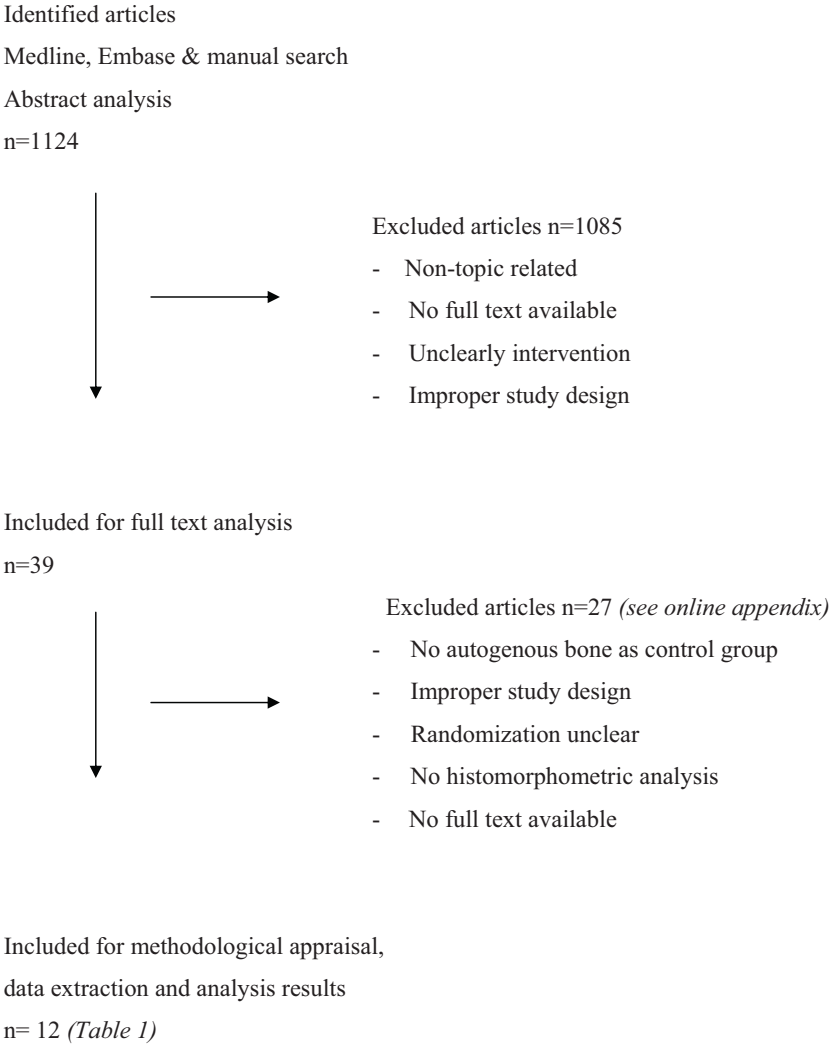


*Fig. 1.* Steps in the systematic review.

the study selection procedure. Articles which were not topic related, with no full texts were excluded. Also studies with an improper study design or an unclear intervention, case series, technical reports and reviews were excluded ($n = 1085$). The $\kappa$-value for inter-reviewer agreement on the methodological appraisal was 0.85. Disagreement was generally caused by slight differences in interpretation and was easily resolved in a consensus discussion.

39 articles were selected for full-text analysis. Of these, 27 further articles had to be excluded because they did not satisfy the inclusion criteria (see the appendix available online). These articles were excluded because of inadequate study design (not longitudinal, not prospective or unclear description of randomization), for not executing histomorphometric analysis or for not including autogenous bone as a control group (details of the excluded studies are given in the online appendix). Authors who did not describe randomization clearly were contacted via e-mail for additional information. When a proper randomization procedure was applied, these studies were added to the results[1,11,21,28].

The 12 articles that fulfilled the inclusion criteria were randomized clinical trials and had applied a split mouth design. There were considerable differences in the selected articles regarding the number of patients, residual bone height, graft materials used, whether implants were placed or not and follow-up. There were some differences in data reporting and in inclusion and exclusion criteria in the studies.

### Description of studies

In all eligible maxillary sinus floor elevation studies autogenous bone was used as a control group. The three types of intervention were: solely bone substitutes; autogenous bone in combination with bone substitutes; autogenous bone in combination with growth-factors. Outcome measures were bone fraction after healing period and implant survival.

In the studies included, patients had been treated with autogenous bone, autogenous bone in combination with bone substitutes or PRP (Table 1). In 5 of the 12 studies, the patients were edentulous, in the others edentulous and dentate patients were treated. In five publications the number of implants placed, the implant survival rate and follow-up was mentioned. To determine an overall survival rate, a comprehensive meta-analysis of these five studies was performed (Table 2).

The morphometric methods for analysing the biopsies used in the included stu-

*Table 1.* Included articles.

| Study | Study design | Control group | Test group | Number of patients | Number of elevations | Number of implants | Biopsies taken | Edentulous/ dentate | Results (bone volume), mean % ± SD | Follow-up | Implant survival rate |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Bettega et al.[2] | RCT split mouth | AB | AB + PRP | $n = 18$ | 36 | 111 | After 6 months | Both | co: 50 (range 38–70) test: 43.2 (range 40–54.8) | 12 months | co: 100% test: 100% |
| Schaaf et al.[24] | RCT split mouth | AB | AB + PRP | $n = 34$* | 68 | ? | After 4 months | Both | co: 35.3 ± 10.7 test: 33.3 ± 11.7 | ? | |
| Consolo et al.[5] | RCT split mouth | AB | AB + PRP | $n = 16$ | 32 | ? | After 4, 5, 6, 7 months | Edentulous | co: 29.2 ± 4 test: 39.9 ± 5.7 | ? | |
| Suba et al.[26] | RCT split mouth | AB | β-TCP (Cerasorb) | $n = 17$ | 34 | ? | After 6 months | Edentulous | co: 34.7 ± 11.9 test: 32.4 ± 10.9 | ? | |
| Raghoebar et al.[22] | RCT split mouth | AB | AB + PRP | $n = 5$ | 10 | 30 | After 3 months | Edentulous | co: 41.1 ± 8.3 test: 38.4 ± 11.3 | 20.2 months | co: 100% test: 96.1% |
| Barone et al.[1] | RCT split mouth | AB | AB + pig bone particles | $n = 18$ | 36 | 90 | After 5 months | Both | co: 70 ± 19.9 test: 67 ± 14.9 | ? | |
| Szabo et al.[27] | RCT split mouth | AB | β-TCP (Cerasorb) | $n = 20$ | 40 | 80 | After 6 months | Edentulous | co: 38.8 ± 7.4 test: 36.5 ± 6.9 | 6 months | co: 95.1% test: 95.1% |
| Zijderveld et al.[40] | RCT | AB | β-TCP (Cerasorb) | $n = 6$* | 12 | 31 | After 6 months | Both | co: 41 ± 10 test: 19.2 ± 5.2 | 11 months | co: 100% test: 100% |
| Zerbo et al.[39] | RCT split mouth | AB | β-TCP (Cerasorb) | $n = 5$* | 10 | ? | After 5 months | Both | co: 41 ± 10 test: 19 ± 5 | ? | co: 100% test: 100% |
| Turunen et al.[35] | RCT split mouth | AB | AB + BG particles | $n = 17$ | 34 | ? | After 4 months | Both | co: 25.1 ± 7.1 test: 25.7 ± 7.4 | 17 months | |
| Hallman et al.[11] | RCT split mouth | AB | AB + Bio-Oss® 20–80% | $n = 11$* | 22 | 68 | After 6 months | Both | co: 37.7 ± 31.3 test: 39.9 ± 8 | 12 months | co: 83.3% test: 94.4% |
| Tadjoedin et al.[28] | RCT split mouth | AB | AB + BG particles | $n = 10$ | 20 | 72 | After 4, 5, 6 months | Edentulous | co: 42.2 ± 4.5 test: 34.5 ± 1.6 | ? | ? |

RCT: randomized clinical trial; AB: autogenous bone; PRP: platelet rich plasma; β-TCP: β-tricalciumphosphates; BG: biactive glass; co: control group; test: test group; ?: no implants placed, therefore also no implant success rate, no follow-up time.

* Only results of patients treated with split mouth design are used.

*Table 2*. Meta-analysis of implant survival rate of included studies.

| Study | Intervention | Number of implants | Follow- up (months) | Exposure time (years and months) | Failures | Failure rate in % | SE_Failure rate in % | Survival rate, 1 year in % |
|---|---|---|---|---|---|---|---|---|
| Bettega et al.[2] | AB | 55 | 12 | 55 years and 0 months | 0 | 0 | 0 | 100 |
| Raghoebar et al.[22] | AB | 15 | 20.2 | 25 years and 3 months | 0 | 0 | 0 | 100 |
| Szabo et al.[27] | AB | 40 | 6 | 20 years and 0 months | 1 | 5 | 5 | 95.1 |
| Zijderveld et al.[40] | AB | 16 | 11 | 14 years and 5 months | 0 | 0 | 0 | 100 |
| Hallman et al.[11] | AB | 33 | 12 | 33 years and 0 months | 6 | 18 | 7.4 | 83.4 |
| Fixed | | | | | | 2.8 | 1.8 | 97.2 |
| Bettega et al.[2] | AB + PRP | 56 | 12 | 56 years and 0 months | 0 | 0 | 0 | 100 |
| Raghoebar et al.[22] | AB + PRP | 15 | 20.2 | 25 years and 3 months | 1 | 4 | 4 | 96.1 |
| Szabo et al.[27] | β-TCP | 40 | 6 | 20 years and 0 months | 1 | 5 | 5 | 95.1 |
| Zijderveld et al.[40] | β-TCP | 15 | 11 | 13 years and 6 months | 0 | 0 | 0 | 100 |
| Hallman et al.[11] | AB + Bio-Oss® | 35 | 12 | 35 years and 0 months | 2 | 5.7 | 4 | 94.5 |
| Fixed | | | | | | 1.8 | 1.1 | 98.2 |

AB: autogenous bone; PRP: platelet rich plasma; β-TCP: β-tricalciumphosphate; SE: standard error; exposure time: calculated by multiplying the mean follow-up time by the number of implants available.

dies were comparable. Quantitative and qualitative investigations of the biopsies were performed with light microscopy and a computerized image analysis system was applied to analyse bone formation in the histological sections.

### Histomorphometric results

Quantitative data analysis (bone fraction) of the data provided in the 12 studies was executed. Bone fraction was defined as the percentage of the total bone fraction. In the various meta-analyses performed, results 5 months after sinus floor augmentation were used because most included studies showed histomorphometric results after 5–6 months.

Regarding PRP, Consolo et al.[5] showed a significant difference in bone fraction in areas reconstructed with a combination of autogenous bone and PRP (40%) or solely with autogenous bone (29%) at 4 and 5 months after sinus floor elevation. Biopsies taken after 6 and 7 months did not show any statistical difference. By contrast, Bettega et al.[2], Raghoebar et al.[22] and Schaaf et al.[24] did not observe any significant difference between both treatments, at the 3 and 6 months evaluations. A meta-analysis of the four included articles failed to show a significant effect of PRP, as the calculated pooled difference [95% CI] in bone fraction was −0.398 [−0.796 to −0.001]; ($P = 0.341$).

β-Tricalciumphosphate (Cerasorb) was been used in the intervention groups in the studies by Suba et al.[26], Szabo et al.[27], Zerbo et al.[39] and Zijderveld et al.[40]. A meta-analysis of these revealed a significantly higher bone fraction 5–6 months after treatment when applying autogenous bone ($P = 0.036$). The calculated pooled difference [95% CI] in bone fraction was 0.987 [0.216–1.758]. In the controls, augmented with autogenous bone, the newly formed bone was mostly lamellar, mature bone (80%). In the β-tricalciumphosphate sites, the newly formed bone was at comparable time points more immature and had a predominantly woven character (74%) [39].

Regarding bioactive glass Tadjoedin et al.[28] showed that augmentation with autogenous bone had resulted in a significantly higher bone fraction (42%) than treatment with bioactive glass (35%) 4 and 5 months after sinus floor elevation. Turunen et al.[35] presented comparable results for both groups after 4 months of healing. In the control group 25% of new bone was seen and in the test group 26%. A meta-analysis of the included studies showed no difference in bone fraction ($P = 0.372$), thus treatment with autogenous bone alone was shown to be as good as treatment with a combination from autogenous bone and bioactive glass when allowing for 5 months' healing. The calculated pooled difference [95% CI] in bone fraction was −0.532 [−1.523 to 0.534].

Regarding pig bone, Barone et al.[1] compared autogenous bone with a combination of autogenous bone and pig bone particles. There were no significant differences 5 months after treatment with autogenous bone alone or in combination with pig bone particles when allowing for 5 months' healing (control 70% ± 19.9, test 67% ± 14.9).

Regarding Bio-Oss®, Hallman et al.[11] used autogenous bone in combination with Bio-Oss® (20–80%) in the test group and showed comparable results in both groups 6 months after sinus floor elevation. The corresponding values for the bone fraction area parameter were 38% ± 31.3 (control group) and 40% ± 8 (test group). A third treatment group was composed of patients who accepted the treatment with a two stage sinus lift with 100% Bio-Oss®. The mean healing time for this group was prolonged to an average of 8.5 months because the newly formed bone was too immature after 6 months to provide enough primary stability for dental implant placement. In this group, bone fraction was 42% ± 26.6, after a healing time of 8.5 months. Results from this group are not included in the analysis because it was not compared with an autogenous bone group.

### Implant survival

Implants inserted in grafts composed of bone substitutes alone, bone substitutes combined with growth factors, or a mixture of autogenous bone and substitutes, all achieved a 1-year survival rate as high as implants placed in autogenous bone alone (Tables 1 and 2). The overall implant survival rate from these studies was 97% for the control group treated with autogenous bone alone and 98% for the various test groups (Table 2). Implant survival was defined as the percentage of implants initially placed that was still present at follow-up, 1 year after implant placement and is calculated as 1 − event rate.

## Discussion

From this systematic review of the literature, evaluating studies in which the bone fraction after sinus floor elevation surgery was evaluated by histomorphological analysis, it is obvious that adequate bone formation in a created space (e.g. the space created between the residual maxillary

ridge and the elevated Schneiderian membrane) can be achieved with a variety of materials when a reasonable healing period (5–6 months) is allowed. According to the findings of the present study, there is no clinical evidence for the superiority of autogenous bone grafts over most bone substitutes in sinus floor elevation procedures when allowing for such a healing period. As the iliac crest is commonly used as a donor site for patients who need a bilateral, vertical maxillary sinus lift, replacement of autogenous bone by bone substitutes might decrease the morbidity and discomfort of the grafting procedure from the patient's perspective.

In this study, autogenous bone served as a control group. It has been shown that the bone fraction measured in an area grafted with autogenous bone was comparable to that grafted with (a mixture of autogenous bone and) bone substitutes when allowing for a reasonably long healing period of at least 5 months[11]. A comparable bone fraction is also present in areas grafted with autogenous bone alone after shorter healing periods (3–4 months[23]) thus allowing for earlier implant placement in such sites.

It has been speculated that growth factors that are present in PRP could enhance healing of the grafts and also counteract resorption after augmentation[31]. Various authors concluded that no relevant differences in healing of soft tissues and bone existed between sites reconstructed with autogenous bone and autogenous bone mixed with PRP[2,22,24]. Four trials evaluated the possible advantage of using PRP to accelerate bone healing for sinus augmentation[2,5,22,24]. No clinical benefit could be observed in a meta-analysis of these studies when using PRP, in other words there is no scientific support for justifying its use in application.

Meta-analyses comparing bone fraction after applying β-tricalciumphosphate revealed a significantly higher bone fraction 5–6 months after treatment when applying autogenous bone ($P = 0.036$). Szabo et al.[27] showed after a 6 month healing period comparable results for both groups. Zerbo et al.[39] and Zijderveld et al.[40] concluded that in the controls, augmented with autogenous bone, the newly formed bone was significantly higher than in the β-tricalciumphosphate group after the same healing period.

Bioactive glass, a material that has been shown to be able to bond directly chemically to bone, is a potentially applicable grafting material for reconstructive procedures. When applied in the size range of 300–355 μm, bioactive glass showed osteoconductive properties[28,29]. Turunen et al.[35] showed that the combined use of bioactive glass granules with autogenous bone chips for augmentation of the maxillary sinus floor diminished the amount of bone needed for augmentation and resulted in the same quantity of bone as when autogenous bone chips alone were used. Tadjoedin et al.[28] showed in the control group, using bioactive glass particles in combination with autogenous bone, that new bone formation increased rapidly within 2 months, from 29% at 4 months to 38% at 6 months. As the healing period is sufficiently long (5 months), there are no differences in treatment and bioactive glass particles seem to be a good alternative for autogenous bone.

Barone et al.[1] compared autogenous bone with a combination of autogenous bone and pig bone particles. They found no significant differences, 5 months after treatment with autogenous bone alone or in combination with pig bone particles when allowing a 5-month healing time.

The use of bovine bone (Bio-Oss®) in combination with autogenous bone offers many advantages. First, it allows the volume of the graft to be at least doubled, avoiding the need to harvest large amounts of autogenous bone. This advantage might also apply to other substitutes. Second, the osteoconductive properties of bovine bone act as a scaffold that is essential for bone remodelling. Third, bovine bone is a calcium-deficient carbonate apatite with a crystal size of approximately 10 nm, therefore, the surface area of each graft particle is considerably greater than that of porous bioceramics, making its resorption considerably slower [9]. In addition, Hallman et al.[11] concluded from their clinical and histological study that similar short-term results can be expected when using autogenous bone, bovine hydroxyapatite, or a mixture of both for maxillary sinus floor augmentation and delayed placement of dental implants.

In Table 2 the survival rate of implants is shown. Implant survival rate was defined as the percentage of implants present at the 1-year follow-up. In some studies, no implants were placed, nor did the authors report on the implant survival rate or the follow-up period was less than 1 year. The available data indicate comparable implant survival in areas reconstructed with either autogenous bone alone or bone substitutes in combination with autogenous bone. This is also supported by the results from Nkenke & Stelzle[19]. When using autogenous bone alone, the healing period can be reduced to an average of 3 months, whereas it is at least 5 months when using a bone substitute either alone or in combination with autogenous bone.

Several systematic reviews and meta-analyses have been performed on studies in which patients underwent sinus floor elevation. For example, the objective of the study by Graziani et al.[10] was to review implant survival following sinus floor augmentation procedures with conventional implant placement in the posterior maxilla. This systematic review suggests that implant survival in the augmented maxillary sinus is more variable (36–100%) than that of implants placed in the posterior maxilla (73–100%). This study is restricted because of the limited data from controlled trails comparing implant survival in the augmented maxillary sinus and the posterior maxilla. Pjetursson et al.[20] studied the surfaces of implants and their failure rate. The best results were obtained using rough surface implants (98% implant survival after 3 years). The analysis in the study from Nkenke & Stelzle[19] considered whether autogenous bone is superior to bone substitutes. This study was limited to titanium implants with modified surfaces placed in sites with 6 mm of residual bone height. The evidence provides a low level of support for selection of autogenous bone or bone substitutes.

The reviews published in the international literature did not have such strict inclusion criteria as the current review[7,10,19,20]. In the current systematic review methodological quality was assessed using specific study-design related forms designed by the Dutch Cochrane Collaboration. The results of the previous systematic reviews are limited because studies that were not well designed were included in the analysis, furthermore no autogenous bone group as a control group and/or no split mouth design was generally used to compare different outcomes and healing time was not always taken into account. No homogeneity between the studies can be reached, which limits the analysis of the data.

A limitation of this systematic review might be that studies comparing various types of bone substitutes, but not including autogenous bone as a control, were not included, as the outcome of these studies might be biassed in showing a higher formation of bone with one substitute that might surpass the level of bone growth as observed in other studies by autogenous bone alone. When autogenous bone had been applied in those studies, it might have been the case that it would have performed better than the substitutes studied. Furthermore, histomorphometric analysis was

required to allow for comparison of results. Restrictions of the present review, including multiple confounding variables such as type of implant, membrane application, height of the residual bone, timing of implant placement, patients compliance and habits might have influenced the outcomes [13].

In future, innovative techniques to promote bone healing or induction growth of bone will be introduced. To reconstruct bony defects, for example, adding mononuclear stem cells derived from a bone marrow aspirate to Bio-Oss® has been shown to result in bone forming kinetics comparable to autogenous bone alone, after a healing period of 3–4 months[23,25]. These mononuclear stem cells can differentiate to osteoblasts if they are added to a bony matrix. The use of a grafting material to perform a maxillary sinus floor elevation procedure may become questionable as a recent study has demonstrated that the mere lifting of the sinus mucosal lining and simultaneous placement of implants also can result in bone formation[17]. Currently this technique is only applied for conditions allowing for sufficient primary stability of implants during placement and a sufficient width of the alveolar crest and not for larger reconstruction in a horizontal or vertical direction. Well designed studies will have to be carried out to determine whether this treatment will reliably result in induction of bone growth.

Taking these limitations into account, it can be concluded from the present systematic review of the literature that bone substitutes, such as Bio-Oss®, bioactive glass or corticocancellous pig bone in combination with autogenous bone, form an alternative for autogenous bone alone for reconstructing bony deficiencies in the maxillary sinus region, for supporting dental implants when there is a healing period of at least 5 months. When applying β-tricalciumphosphate, the use of a mixture with autogenous bone is preferred to allow for a short healing period before implant placement. There is no scientific support for adding PRP to autogenous bone or bone substitutes to speed up the healing time of bone. Finally, short-term implant survival, the major clinical outcome, is not influenced by the various grafting procedures applied when allowing for a sufficient healing time before implant placement.

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